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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,805	08/25/2006	Ulrich Kautz	27599U	2179

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EXAMINER	
DESAI, RITA J	
ART UNIT	PAPER NUMBER
1625	
MAIL DATE	DELIVERY MODE
08/20/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,805	KAUTZ, ULRICH	
	Examiner	Art Unit	
	Rita J. Desai	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14,16 and 17* is/are pending in the application.

4a) Of the above claim(s) *16,17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/9/07,,12/12/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 7/1/09 is acknowledged. The traversal is on the ground(s) that there is no lack of unity. This is not found persuasive because the examiner has cited WO99/05111 to indicate that the core of the compounds is not novel and hence not a contribution over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

Specification

The disclosure is objected to because of the following informalities: The formula on page 2 of the specification has the phenyl group which is not bonded to the tricylic core..

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

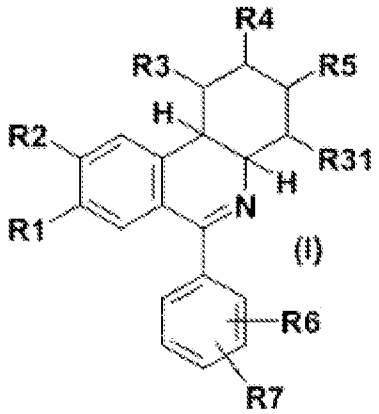
Claims 1-12 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for formula I where in R3, R5, R31 and R6 are H, does not reasonably provide enablement for all these group to be all the various groups as claimed, or for Har1, har 2, het 1, het 2 are groups other than those as given in claims 5 and 6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the invention commensurate in scope with these claims. In re

Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims: The instant claims encompass many compounds of the formula



wherein R1-R6 have many variables and R7 is any heterocyclic group. These compounds cover a very wide range of compounds.

2) The nature of the invention: The invention is a tricyclic compound useful as PDE inhibitors.

3) The state of the prior art: The state of the prior art is that it involves screening in vitro and invivo to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability and no established correlation between in vitro activity and the treatment as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.
Similar compounds as disclosed in WO 99/05111, WO99/05112, WO02/05616 hall have similar compounds with the same activity. None of them have all the other various substituents. **4) The level of one of ordinary skill:** The ordinary artisan is highly skilled.

5) The level of predictability in the art: How to use **:-** It is noted that the pharmaceutical art is unpredictable , requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statue. The level of unpredictability is in the art is very high. The compounds which differ by a methyl group also show different properties, for e.g. theophylline and caffeine. One of them is a bronchodilator and they differ only by a methyl group.

How to make:- As stated in the preface to a recent treatise:

"Most non-chemists would probably be horrified if they wereto learn how many attempted syntheses fail, and how inefficient research chemists are. The ratio of successful to unsuccessful chemical experiments in a normal research laboratory is far below unity, and synthetic research chemists, in the same way as most scientists, spend most of their time working out what went wrong, and why. Despite the many pitfalls lurking in organic synthesis, most organic chemistry textbooks and research articles do give the impression that organic reactions just proceed smoothly and that the total synthesis of complex natural products, for instance, is maybe a labor-intensive but otherwise undemanding task. In fact, most syntheses of structurally complex natural products are the result of several years of hard work by a team of chemists, with almost every step requiring careful optimization. The final synthesis usually looks quite different from that originally planned, because of unexpected difficulties encountered in the initially chosen synthetic sequence. Only the seasoned practitioner who has experienced for himself the many failures and frustrations which the development (sometimes even the repetition) of a synthesis usually implies will be able to appraise such work .....Chemists tend not to publish negative results, because these are, as opposed to positive results, never definite (and far too copious) ....." Dorwald F. A.

Side Reactions in Organic Synthesis, 2005, Wiley: VCH, Weinheim pg. IX of Preface.

6) The amount of direction provided by the inventor: The inventor provides some compounds with R3, R5, R31 and R6 being H, and R7 being limited hetero groups. There are no examples with all the various hetero groups and all the various substituents for R3, R5 , R31 and R6.

7) The existence of working examples: The instant specification does not have any working examples for these various substituents. Nor are there similar substitutents on the prior art compounds . There is no activity data given for this scope.

8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: Since there are no working examples, the amount of experimentation to make and use these compounds is very high and burdensome.

Taking the above eight factors into consideration, it is not seen where the instant specification enables the ordinary artisan to make and/or use the instantly claimed invention.

Genetech Inc Vs Nova Nordisk 42 USPQ 2d 1001.

"A patent is not a hunting license. It is not a reward for search but compensation for its successful conclusion and patent protection is granted in return for an enabling disclosure of an invention , not for vague intimations of general ideas that may or may not be workable."

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that,

based on the evidence regarding each of the above factors, the specification, at the time the application was flied, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over

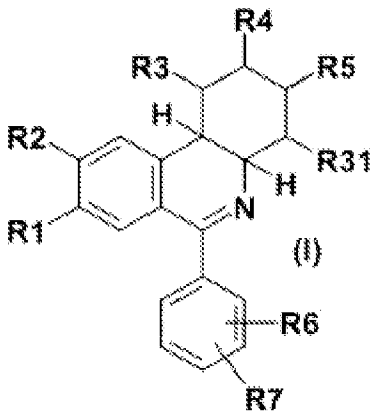
WO 99/05111 Amschler et al and

WO02/05616 Bundschun et al .

WO 2004/019945 Flockerzi et al

WO 2005077906 102(e). (all references are cited on the IDS)

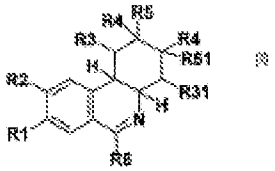
Applicants compounds are drawn to the compounds of the formula



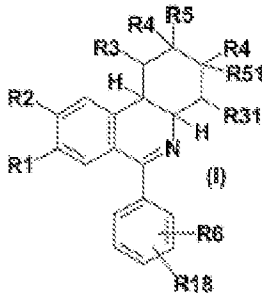
wherein R4 is an -O linked group and R7 is a het group.

Scope & Content of Prior Art MPEP 2141.01

The reference WO 99/05111 discloses compounds of the invention .



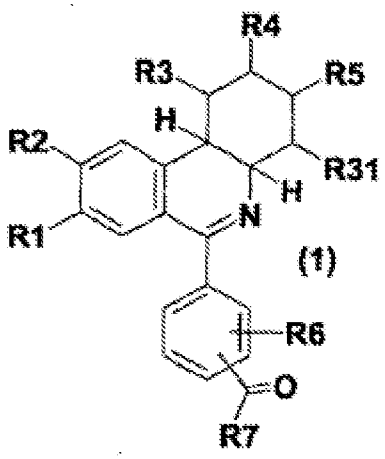
See example 1 page 13. R7 is a tetrazol, positions 9 and 8 are alkoxy,.



WO 02/05616 discloses compounds

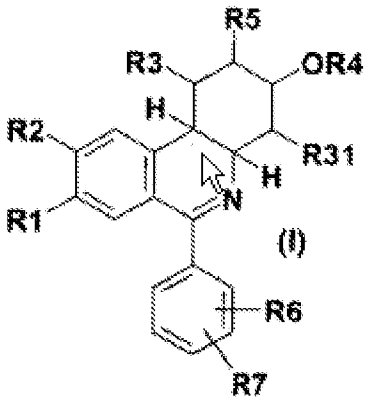
generically with R6 being a tetrazole.

WO 2005077906 (102(e) date 2/18/04



R4 is an OR41

WO 2004/019945 102(e) date 29 Aug 2002. discloses compounds of similar core with a OR4



All these compounds have the same activity of PDE inhibitors.

Difference between Prior Art and the claims MPEP 2141.02

The difference between the prior art and applicants compounds is the specific substitutents of the R4, R5 groups along with the R7 being a het group.

Prima Facie Obviousness , Rational and Motivation MPEP 2142-2413

The 3 prior art references have the same core and similar activity. The R4 or R5 being an -OR group is shown in the '616 reference. The WO'111 reference teaches the R7 to be a het group, tetrazole to be specific. The WO '996 and '905 reference further teaches a that the R4 or R5 can be an –OR group and still retain its properties.

In view of the several reference which have similar properties and a similar core , making minor modifications such as an OH group at a different location or a substitutent on the phenyl group and expect the compounds to retain its properties is motivation for a person of skill in the

art to try and modify the compounds. There is no showing of unexpected results to show that the compounds are unobvious over those of the prior art.

A compound that differs only in molecular arrangement from the compounds disclosed in the prior art and which for which no unexpected properties of this compound are disclosed in the specification is unpatenable, *Ex parte KRUEGER AND HAYES*, 121 USPQ 420, *In re NORRIS*, 84 USPQ 458, *In re Hass* 60 USPQ 552, which found a *prima facia* case of obviousness of 1-chloro-1-nitrobutane over 1-chloro-1-nitroisobutane taught in the prior art, *Ex parte Ullyot*, 103 USPQ 185, which found a *prima facia* case of obviousness of 2-oxo-quinolines over a 1-oxo-isoquinoline taught in the prior art, *In re FINLEY,* 81 USPQ 383 , which found a *prima facia* case of obviousness of 2-ethyl hexyl salicylate over octyl salicylate taught in the prior art.

For example, "Position isomerism has been used as a tool to obtain new and useful drugs" (*Englehardt*) and "Position isomerism is fact of close structural similarity" (*Mehta*, emphasis in the original). Note also *In re Jones,* 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to prima facie obviousness"; one of those listed is "adjacent homologues and structural isomers". Position isomers are the basic form of close "structural isomers." *In re Deuel* 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds…a known compound may suggest it analog or isomers, either geometric (cis v. trans) or position isomers (e.g. *ortho v. para*)."

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-12 and 14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 7329676. and 6,121279, US 6,127, 378, US 6,191,138, US 6,410,551, US 6,476,025, US 6,306,869 Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent discloses a similar core with the OR4 group and in view of the other patents ,US 6,121279, US 6,127, 378, US 6,191,138, US 6,410,551, US 6,476,025, US 6,306,869 which again disclose the same core and isomers.

Claims 1-12 and 14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim s 1-8 of copending Application No. 11/884934. Although the conflicting claims are not identical, they are not patentably distinct from each other because these compounds have the same core and same use.

See above 103 rejection. Similar compounds are expected to have similar properties in the absence of unexpected results.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The double patenting also applies to application numbers 11/590,803, 10/591472,, 11/795981, 10/524820 (or 7329676), 11/885423 as they, in combination are obvious.

All these application have the same core and same use. 11/884934 also teaches the heteroring on the phenyl groups.US 7329676 teaches the OR4 groups and has the same activity. Thus all the variables are taught and applicants have similar core and same use and so one of skill in the art would be motivated to modify and find it obvious to try to make these compounds with a predictable result.

The applicants have many prior applications drawn to compounds with the same core and same activity, appearing that the activity is due to the core. Slight modifications of the substituents from one position to the other would be obvious to try and in the absence of unexpect results is prima facie obvious and not patentable.

Conclusion

Claims 1-12 and 14 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

August 13, 2009